Epilepsy Treatment Priorities: Answering the questions that matter

Emily G Hughes,[1] Rhys H Thomas[2,3]

Emily G Hughes

HughesE17@cardiff.ac.uk

1. School of Medicine, UHW Main Building, Heath Park, Cardiff, CF14 4XN, United Kingdom.

Rhys H Thomas

ThomasRh5@cardiff.ac.uk

2. Department of Neurology, University Hospital of Wales, Heath Park, Cardiff, CF14 4XW, United Kingdom

3. Institute of Psychological Medicine and Clinical Neurosciences, Hadyn Ellis Building, Maindy Road, Cardiff University, CF24 4HQ, United Kingdom

Words: abstract 200 / main body 990

Key words: Epilepsy, choice, partnership, drugs, uncertainty

Epilepsy Treatment Priorities: Answering the questions that matter

EG Hughes, RH Thomas

Abstract

Objective To identify research priorities that have been answered, six years after being identified as important to people with epilepsy and epilepsy professionals.

Background The DUETs database collates key unanswered questions identified by patients and professionals. In 2011, 398 questions were created using focus group methodologies. We wanted to know whether published research has since answered these important questions.

Design The top 20 ranked questions for both patients and clinicians were studied. The PubMed and Cochrane databases were searched for published papers and NICE, SIGN and ILAE guidance for authoritative statements. The number of papers targeted at answering these research priorities was recorded.

Results The questions from epilepsy professionals yielded 356 papers, 158 answering the topic. Patients' questions yielded 150 papers, of which 73 targeted the priorities. All professionals' questions were answered by a paper or guideline, as opposed to 75% of patients' questions.

Conclusions Researchers are doing a fine job at answering research priorities that are of interest to them and their peers. Unanswered and important research priorities produced by patients and carers produce 46% as many papers, are addressed in 24% as many guidelines, or go unanswered entirely.

Introduction

"Nothing about them, without them" is the clarion call of those who are committed to genuine user participation in research. The James Lind Alliance, brings patients, carers and clinicians together as priority sharing partnerships to ensure that research is targeted at questions that matter to these interested parties. In 2010 we contributed to the database of uncertainties of the effects of treatments (DUETS). 398 questions regarding treatments and their effects were produced from focus groups comprised of people with epilepsy, their carers and relatives – or epilepsy clinicians and researchers.[1] The questions were subsequently ranked by participants and thematically grouped to identify similarities and comparisons. The top ranked questions were all deemed 'unanswered' at the time of publication following thorough scrutiny of online databases.[2] It was our hope by publishing the report and by uploading all questions to the NHS Evidence DUETs webpage [2] that we would encourage researchers to preferentially focus on these questions. Epilepsy was one of the first partnership exercises to be launched and we aim to assess the influence of the process since the priorities were published. We sought to identify if the top 20 ranked questions from professionals and patients had been answered over the last six years (supplementary data).

Methods

We searched the PubMed and Cochrane databases for published papers, and NICE, SIGN, ILAE, AES, NCS and EFNS guidance for authoritative statements (from January 1st 2010 to April 1st 2016). Papers were rated as 'answering' a question if they contained new data that wholly or in part addressed the uncertainty. Review articles, most case reports and hypotheses without data were not included. We recorded the total number of papers yielded by the search strategy and the number that answered the question.

Results

Clinicians and Researchers				Patients and Carers			
Question Rank	**Relevant papers identified**	**Papers answering question**	**Guidelines answering question**	**Question Rank**	**Relevant papers identified**	**Papers answering question**	**Guidelines answering question**
1	63	33	2 - NICE, SIGN	**1**	27	24	0
2	3	1	2 - NICE, SIGN	**2**	2	2	1 – NICE
3	36	20	1 - SIGN	**3**	50	11	1 – NICE
4	1	1	0	**4**	Answered by question 1		
5	9	3	0	**5**	6	4	0
6	10	0	1 - SIGN	**6**	2	1	0
7	Answered by question 1			**7**	12	4	2 – NICE, SIGN
8	21	12	0	**8**	2	2	1 – SIGN
9	8	4	1 - SIGN	**9**	19	15	0
10	Answered by question 8			**10**	0	0	0
11	96	39	5 - NICE, SIGN, AESG, NCS, EFNS	**11**	1	1	0
12	Answered by question 11			**12**	5	2	0
13	12	7	3 - SIGN, NCS, EFNS	**13**	0	0	0
14	0	0	1 - NICE	**14**	22	6	0
15	9	3	1 - SIGN	**15**	Answered by question -3		
16	31	12	2 - NICE, SIGN	**16**	2	1	0
17	17	5	1 - SIGN	**17**	0	0	0
18	9	5	2 - NICE, SIGN	**18**	0	0	1 – SIGN
19	22	11	1 - SIGN	**19**	0	0	0
20	9	2	2 - NICE, SIGN	**20**	0	0	0

Table 1. The number of papers found relating to each question formulated by clinicians and researchers, and patients and carers, are listed. This number is split into the total number of papers identified by the search strategy, and the number of papers with new data relevant to the question that addresses each question. The guidelines relating to each question are also shown. The clinician

questions clustered in several groups: prescribing in pregnancy (1, 7, 9, 20); prescribing choices and drug withdrawal (2, 4, 6, 14, 18); cognitive and psychiatric side effects (5, 15, 17, 19); non-epileptic attack disorder (8, 10); and status epilepticus (11, 12, 13). Patient questions clustered into themes about education (1, 4, 12); cognitive and psychiatric side effects (3, 5, 9, 15, 18); how to take medication and AED monitoring (2, 6, 7, 10, 17); and epilepsy service configuration (6, 20).

Clinicians and researchers

Three questions were adequately addressed by a similar question, leaving 17 unique questions (table 1). The status epilepticus questions had the most papers addressing them - 46 targeted papers from a total of 108 identified. 'Prescribing in pregnancy' and 'cognitive and psychiatric effects' were next best answered, with 39 and 22 targeted papers respectively. Question 9, 'Should the lamotrigine dose be pro-actively increased in pregnancy?', is the focus of an ongoing trial: EMPiRE Study – Anti-Epileptic drug Monitoring in PREgnancy: an evaluation of effectiveness, cost-effectiveness and acceptability of monitoring strategies.[3] We identified no relevant papers for two questions (6 and 14).

Patients and carers

The top 20 questions from patients and carers produced 18 unique uncertainties (table 1). The top priority was addressed. The clusters that involved allied health professionals such as education (26 targeted papers) and cognition and psychiatric effects (30 papers) were better answered than practical questions about how best to take the medication, and service configuration (7 and 1 papers respectively).

There were 158 relevant papers for the clinicians' and researchers' questions (mean 9.3 per question, range 0-39) compared to 73 for the patient and carers' questions (4.1 per question, range 0-24). There was a trend for the questions to get less well answered as the question's ranking dropped. Fewer patient questions were addressed by national guidelines than the professionals'

questions (6 vs 25). All of the professionals' questions were answered by research or guidelines, compared to 15 of the patients' questions.

Discussion

We recognise that our research strategies were not exhaustive and were unblinded. We demonstrate that researchers could be doing more to answer the questions that matter to patients with epilepsy. In contrast researchers are doing a fine job at answering research priorities that are of interest to them and their peers. Research priorities produced by patients and carers produce only 46% as many papers, are addressed in only 24% as many guidelines, and often go unanswered entirely. This is despite patient questions often being more tangible and practical. Many of these practical questions remain entirely unanswered. Interestingly, with question 18 (over diagnosis of depression in epilepsy), there was much new research about the link between epilepsy and depression, but no results specifically answering the patients' question. This indicates that research in this area is happening, but not being focussed to areas with keen patient interest.

We suspect that many of the professionals' questions were created and rated highly because they were aware of the literature, ongoing research, and because they keep up-to-date with controversies. In contrast, many of the patients' questions do not have the research momentum and appear de novo. Many of these questions could be considered partially answered, and now it would be useful to create a more specific list of questions relating to each of the broadly 'answered' topics. Examples of true evidence gaps are management when initial epilepsy treatment fails, and how effective second line treatment is, following initial treatment failure.

Other priority setting partnerships using the DUETs model have looked at the dissemination and impact of their priorities. The childhood disability group asked the Health Technology Assessment (HTA) and Health Services and Delivery Research (HS&DR) programmes to identify which of their top

questions were the focus of successful funding awards.[4] A year after publication, two were being answered: the top priority regarding therapeutic regimens, the tenth focussing on sleep disturbance; and a third was the subject of NICE guidance in preparation. The Palliative Care group's priorities gained immediate traction within their community.[5] The All Ireland Institute of Hospice and Palliative Care arranged a local prioritisation workshop, to reprioritise the longlist to their local circumstances. Using the UK Clinical Research Collaboration (UKCRC) database they undertook a research mapping exercise to identify the grants that may answer their top questions. They have taken the process further by both reviewing the out of scope questions and, with the Motor Neurone Disease Association, directly commissioning research that answers their longlist of priorities. We suggest that it is time for a new epilepsy priority sharing partnership to be convened using the James Lind Alliance model and we hope that the priorities that they produce can capture the imaginations of charities, grant administering bodies and researchers.

Acknowledgements

We are grateful to the patients, their relatives and carers, the clinicians and scientists who gave up their time to participate in the original study.

Funding

This study was not directly funded.

Competing interests

EH has nothing to report. RHT receives/has received research support from Epilepsy Research UK, Action Medical Research, Epilepsy Action and the Dravet Society; is an associate editor of Practical Neurology and web editor of Seizure; he has received honoraria from Eisai, Sanofi and UCB.

References

[1] Thomas RH, Hammond CL, Bodger OG, Rees MI, Smith PE; members of WERN & James Lind Alliance. Identifying and prioritising epilepsy treatment uncertainties. J Neurol Neurosurg Psychiatry. 2010;81(8):918-21.

[2] Database of Uncertainties about the Effects of Treatment. What is UK DUETs? 2016 [accessed 28 Sept 2016]. Available from: www.library.nhs.uk/duets/

[3] National Institute for Health Research. Antiepileptic drug (AED) management in pregnancy: an evaluation of effectiveness, cost effectiveness and acceptability of dose adjustment strategies. 2011 [accessed 28 Sept 2016]. Available from: www.nets.nihr.ac.uk/projects/hta/095538

[4] Morris C, Simkiss D, Busk M, et al. Setting research priorities to improve the health of children and young people with neurodisability: a British Academy of Childhood Disability-James Lind Alliance Research Priority Setting Partnership. BMJ Open. 2015;5(1):e006233.

[5] Putting patients, carers and clinicians at the heart of palliative and end of life care research [Internet]. Palliative and end of life care Priority Setting Partnership (PeolcPSP); 2015 [cited 28 Sept 2016]. Available from: www.palliativecarepsp.org.uk/wp-content/uploads/2015/01/PeolcPSP_Final_Report.pdf